

# **EXHIBIT 5**

ORIGINAL RESEARCH

**OPEN ACCESS**

Full open access to this and thousands of other papers at <http://www.la-press.com>.

## A Finished Dietary Supplement Stimulates Lipolysis and Metabolic Rate in Young Men and Women

Cameron G. McCarthy, Tyler M. Farney, Robert E. Canale, Rick J. Alleman Jr. and Richard J. Bloomer

Cardiorespiratory/Metabolic Laboratory, Department of Health and Sport Sciences, University of Memphis, Memphis, TN, USA. Corresponding author email: [rbloomer@memphis.edu](mailto:rbloomer@memphis.edu)

**Abstract**

**Background:** Dietary supplements are often marketed to increase lipolysis and thermogenesis, with the proposed end result being weight loss and body fat reduction. It was the purpose of the present investigation to study the acute effects of a weight/fat loss supplement within a sample of healthy human subjects.

**Methods:** Twelve subjects (men  $24.8 \pm 4.3$  yrs; women  $22.8 \pm 0.4$  yrs) ingested a dietary supplement (OxyELITE Pro™) or a placebo, on two separate days in a double-blind, cross-over design. Blood samples were collected immediately before ingestion, and at 60 and 120 minutes post ingestion, and analyzed for plasma glycerol and free fatty acids (FFA). Breath samples were collected immediately before ingestion and at 30, 60, 90, and 120 minutes post ingestion, for a measure of kilocalorie expenditure using indirect calorimetry. Area under the curve (AUC) was calculated. Heart rate and blood pressure were recorded at all times and rate pressure product (RPP) was calculated.

**Results:** AUC was greater for supplement compared to placebo for glycerol ( $22.74 \pm 1.98 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$  vs.  $15.76 \pm 1.36 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ ;  $P=0.001$ ), FFA ( $1.62 \pm 0.07 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$  vs.  $0.78 \pm 0.12 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ ;  $P < 0.0001$ ), and kilocalorie expenditure ( $149 \pm 7 \text{ kcal} \cdot 2 \text{ hr}^{-1}$  vs.  $122 \pm 8 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ ;  $P=0.005$ ). Heart rate ( $P=0.02$ ), systolic blood pressure ( $P < 0.0001$ ), and RPP ( $P=0.002$ ) were higher for supplement compared to placebo.

**Conclusion:** Ingestion of OxyELITE Pro™ resulted in an increase in blood markers of lipolysis, as well as metabolic rate, during a two-hour post ingestion time period. An increase in hemodynamic variables was also observed. These findings are in reference to a sample of healthy men and women who were naïve to treatment with the dietary supplement. Additional work is needed to determine if the acute changes observed here would persist with chronic use of the supplement and possibly lead to weight/body fat loss over time.

**Keyword:** lipolysis, supplements, weight loss, thermogenesis

*Nutrition and Metabolic Insights* 2012:5 23–31

doi: [10.4137/NMI.S8567](https://doi.org/10.4137/NMI.S8567)

This article is available from <http://www.la-press.com>.

© the author(s), publisher and licensee Libertas Academica Ltd.

This is an open access article. Unrestricted non-commercial use is permitted provided the original work is properly cited.



## Background

Obesity and overweight status has increased significantly in recent years, with an estimated 400 million individuals classified as obese,<sup>1,2</sup> and 1.6 billion classified as overweight.<sup>2</sup> While the optimal treatment plan for this epidemic likely includes increased physical activity coupled with modification and restriction in dietary intake, many individuals choose rather to focus on the use of pharmaceuticals or dietary supplements. In most industrialized nations, dietary supplements are big business. In fact, the supplement industry has been following an increasing sales trend since 2004 and was worth \$61 billion to the United States economy in 2008, with an estimated 80 percent of adults purchasing supplements at least once per year.<sup>3</sup> Dietary supplements designed to aid in body weight/fat loss are one of the more popular classes of products sold, estimated to be a 700 million dollar industry in 2008.<sup>4</sup>

Unfortunately, most weight/fat loss supplements have little to no scientific support, in particular as pertaining to their use by human subjects. Moreover, some have been reported to cause ill-health.<sup>5</sup> As with many dietary supplements, those within the weight/fat loss category are often formulated based on results obtained from studies using isolated ingredients. While this alone is not problematic, the concern lies in the fact that most ingredients have only been studied in animals and not in human subjects, and the dosages used in such animal trials are often far greater than those used in finished products marketed to humans.

OxyELITE Pro™ is a dietary supplement marketed as a weight/fat loss aid. As with most dietary supplements, this product contains a combination of several ingredients purported to increase one or more aspects of metabolic rate or lipolysis, some of which have not yet been investigated in human subjects. Specifically, this product contains a proprietary blend of caffeine, baubinia purpurea, bacopa monniera, geranium stem extract (1,3-dimethylamylamine), cirsium oligophyllum, and rauwolschine extract as the active ingredients.

With the exception of caffeine, which has been investigated extensively in human subjects,<sup>6,7</sup> to our knowledge, little objective scientific evidence is available pertaining to the other ingredients as used by human subjects. It was our intention in the present study to investigate the acute effects of this

supplement on blood markers of lipolysis, as well as metabolic rate. While we understand the need to conduct long-term intervention studies pertaining to the potential effect of this supplement on weight/fat loss over time, it was the purpose of the present study to first determine if the product resulted in an acute increase in our selected outcome measures. If so, then follow-up intervention studies would be warranted.

## Methods

### Subjects

Healthy, exercise-trained men ( $n = 6$ ) and women ( $n = 6$ ) participated in this study. All subjects completed a medical history and physical activity questionnaire. No subject smoked cigarettes or had diagnosed disease of cardiovascular or metabolic origin. Men and women were very active and considered to be exercise-trained, as they performed combined aerobic and anaerobic exercise for an average of 7 and 5 hours per week, respectively, for the past several years. Subject descriptive characteristics are presented in Table 1. All experimental procedures were performed in accordance with the Helsinki Declaration. The University of Memphis Human Subjects Committee approved all experimental procedures. Subjects provided verbal and written consent prior to participating in this study.

**Table 1.** Characteristics of 6 men and 6 women.

Variable	Men	Women
Age (yrs)	24.8 ± 4.3	22.8 ± 0.4
Height (cm)*	179.3 ± 6.6	166.0 ± 9.0
Weight (kg)*	81.1 ± 11.6	62.3 ± 12.6
BMI (kg · m <sup>-2</sup> )	25.5 ± 5.0	22.4 ± 2.6
Body fat (%)*	14.7 ± 7.6	25.5 ± 3.1
Waist (cm)	84.6 ± 12.1	77.2 ± 6.8
Hip (cm)	102.6 ± 8.6	95.7 ± 6.6
Waist:hip	0.82 ± 0.05	0.81 ± 0.08
Years anaerobic exercise training	3.0 ± 3.6	2.2 ± 2.3
Hours per week anaerobic exercise	3.5 ± 2.7	1.6 ± 1.9
Years aerobic exercise training	1.6 ± 1.3	2.1 ± 1.6
Hours per week aerobic exercise	3.2 ± 2.0	3.4 ± 1.1

**Notes:** Data are mean ± SD. \*Statistically significant difference noted in height ( $P = 0.01$ ), weight ( $P = 0.02$ ), and body fat ( $P = 0.01$ ). No other statistically significant differences noted ( $P > 0.05$ ).



## Conditions and testing

Following screening procedures, subjects reported to the lab in the morning hours (0600–0900) on two different occasions separated by 3–4 days, to undergo testing. The time of day for testing was matched for each subject. Procedures described below were identical for both test sessions (supplement and placebo). The dietary supplement used in this investigation (OxyELITE Pro™; USPlabs, LLC; Dallas, TX) contained a proprietary blend of caffeine, baubinia purpurea, bacopa monniera, geranium stem extract (1,3 dimethylamylamine), cirsium oligophyllum, and rauwolfscine extract as the active ingredients. Capsules were from the same bottle and produced in accordance with Good Manufacturing Practices. Subjects ingested two capsules of the dietary supplement, or an identical looking placebo (microcrystalline cellulose). The experiment was conducted as a double blind, cross-over design. No other food was allowed during the two hour post intake period. However, water was allowed ad libitum, and was measured and matched for both days of testing (mean intake for men = 525 mL; mean intake for women = 317 mL).

Subjects reported to the laboratory in a fasted state ( $\geq 10$  hours), without caffeine consumption during the past 10 hours. Subjects were asked not to exercise or to perform any strenuous physical activity for the 24 hours prior to each testing day. Following a 10 minute rest period, heart rate (via monitor) and blood pressure (via auscultation) were measured (rate pressure product was calculated as:  $HR \times SBP = RPP$ ), a blood sample was obtained, and subjects provided a five minute breath sample (for analysis of metabolic rate). Subjects then ingested either the supplement or placebo, in the presence of an investigator. At all other measurement times (30, 60, 90, and 120 minutes post ingestion), the same order of collection as described above was followed; however, blood was only collected at 60 and 120 minutes post ingestion. Subjects remained inactive in the laboratory during the entire two hour test period.

The measurement of metabolic rate was performed using indirect calorimetry via breath-by-breath collection (SensorMedics V<sub>max</sub> 229 metabolic system; Yorba Linda, CA). All gas collection took place in a temperature and humidity controlled laboratory. The flow sensor and gas analyzers were calibrated prior to data collection each day. Total oxygen consumption

( $L \cdot \text{min}^{-1}$ ) was determined from gas collection and total kilocalorie expenditure was estimated from this value. The respiratory exchange ratio (RER) was also determined from gas collection data ( $VCO_2/VO_2$ ), and used as a measure of substrate utilization.

## Blood collection and biochemistry

A total of three venous blood samples (7 mL per draw) were taken from subjects' forearm via needle and Vacutainer® (pre ingestion, 60, and 120 minutes post ingestion). Blood was immediately processed in a refrigerated centrifuge in order to obtain plasma (4 °C for 15 min at  $2000 \times g$ ). Plasma samples were then stored in multiple aliquots at  $-70$  °C. Assays were performed in duplicate on first thaw within four weeks of sample collection. Glycerol was determined using the Free Glycerol Determination Kit (FG0100) and Glycerol Standard (G7793), following the instructions of the manufacturer (Sigma Aldrich; St. Louis, MO). Free fatty acids (FFA) were determined using the Free Fatty Acid Quantification Kit (K612-100) following the instructions of the manufacturer (BioVision; Mountain View, CA).

## Dietary intake

Subjects were required to record all food and drink consumed during the 24 hour period prior to the initial test day. Records were then copied and returned to subjects so that they could attempt to mimic this intake during the 24 hour period prior to the second test day. Records were analyzed for total calories, protein, carbohydrate, fat, and a variety of micronutrients (Food Processor SQL, version 9.9, ESHA Research, Salem, OR).

## Statistical analysis

Area under the curve (AUC) was calculated for biochemical and metabolic data using the trapezoidal method ( $AUC_G$ ) as described in detail by Pruessner et al<sup>8</sup> Statistical comparisons for biochemical ( $AUC_G$ ) and metabolic data were made using a  $2$  (sex)  $\times$   $2$  (condition) repeated measures analysis of variance (RMANOVA). Biochemical, metabolic, and hemodynamic (% change) data were also compared using a sex  $\times$  condition  $\times$  time RMANOVA. Tukey's *post hoc* testing was used when needed. All analyses were performed using JMP statistical software (version 4.0.3, SAS Institute, Cary, NC).



Statistical significance was set at  $P \leq 0.05$ . The data are presented as mean  $\pm$  SEM, except for subject descriptive characteristics (mean  $\pm$  SD).

## Results

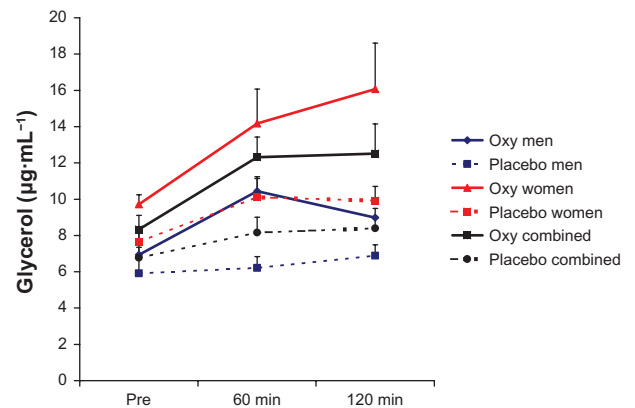
### Subject characteristics, dietary data, and subjective response to supplement

Expected differences were noted between men and women for selected anthropometric variables (Table 1). The same was true of dietary intake of kilocalories ( $P = 0.0006$ ), protein ( $P < 0.0001$ ), carbohydrate ( $P = 0.008$ ), and fat ( $P = 0.008$ ), with men consuming more than women.

Most importantly, no differences were noted between conditions for total kilocalorie intake, protein, carbohydrates, fat, vitamin C, vitamin E, or vitamin A consumption during the 24 hours prior to each test day ( $P > 0.05$ ). Dietary data are presented in Table 2. In terms of subjective response to treatment with the supplement, some subjects reported feeling “jittery”, “on-edge”, “sweaty”, and “shaky”, sometimes involving cold sweats, a racing heart beat, and poor sleep quality on the night of treatment.

### Biochemical data

When considering the AUC analysis, no sex  $\times$  condition interactions were noted for glycerol ( $P = 0.53$ ) or FFA ( $P = 0.08$ ). However, a condition ( $P = 0.001$ ) and sex ( $P = 0.0007$ ) effect was noted for glycerol, with values higher for supplement compared to placebo and higher for women compared to men. Data are presented in Figure 1. A condition ( $P < 0.0001$ ), but not sex ( $P = 0.85$ ) effect was noted for FFA, with values higher for supplement compared to placebo. Data are presented in Figure 2.



**Figure 1.** Plasma glycerol before and following ingestion of placebo and OxyELITE Pro™ by men and women.

**Notes:** Data are mean  $\pm$  SEM. Sex  $\times$  Condition  $\times$  Time:  $P = 0.43$ ; Sex  $\times$  Time:  $P = 0.25$ ; Condition  $\times$  Time:  $P = 0.21$ ; Sex  $\times$  Condition:  $P = 0.23$ ; Time:  $P = 0.001$  (60 min and 120 min higher than Pre;  $P < 0.05$ ); Condition:  $P < 0.0001$ ; Sex:  $P < 0.0001$ ; **Area under the curve.** Sex  $\times$  Condition:  $P = 0.53$ ; Condition:  $P = 0.001$ ; Sex:  $P = 0.0007$ ; OxyELITE Pro™ Men:  $18.40 \pm 0.77 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ ; Placebo Men:  $12.61 \pm 1.12 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ ; OxyELITE Pro™ Women:  $27.07 \pm 3.01 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ ; Placebo Women:  $18.90 \pm 1.73 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ ; OxyELITE Pro™ Combined:  $22.74 \pm 1.98 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ ; Placebo Combined:  $15.76 \pm 1.36 \mu\text{g} \cdot \text{mL}^{-1} \cdot 2 \text{ hr}^{-1}$ .

### Metabolic data

When considering the AUC analysis for kilocalories, no sex  $\times$  condition interactions were noted ( $P = 0.26$ ). However, a condition ( $P = 0.005$ ) and sex ( $P = 0.002$ ) effect was noted, with values higher for supplement compared to placebo and higher for men compared to women. Data for kilocalories are presented in Figure 3 and data for RER are presented in Figure 4.

### Hemodynamic data

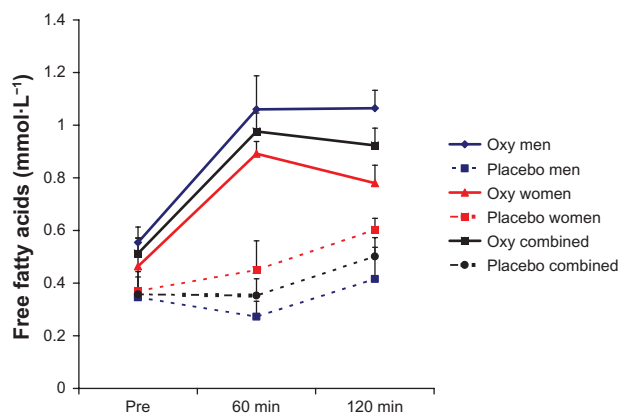
Several differences were noted for both absolute and percent change data for hemodynamic variables. Absolute data are presented in Tables 3, 4, 5, and 6. Percent change data are presented in Figures 5 and 6.

**Table 2.** Dietary data of 6 men and 6 women during the 24 hour period before ingestion of placebo and OxyELITE Pro™.

Variable	Men		Women		Combined	
	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo
Kcal	2582 $\pm$ 376	2972 $\pm$ 353	1477 $\pm$ 245	1482 $\pm$ 277	2030 $\pm$ 271	2227 $\pm$ 310
Protein (g)	124 $\pm$ 18	131 $\pm$ 12	63 $\pm$ 7	63 $\pm$ 11	93 $\pm$ 13	97 $\pm$ 13
Carbohydrate (g)	368 $\pm$ 74	394 $\pm$ 69	207 $\pm$ 39	210 $\pm$ 43	287 $\pm$ 47	302 $\pm$ 48
Fat (g)	71 $\pm$ 9	98 $\pm$ 19	47 $\pm$ 10	47 $\pm$ 9	59 $\pm$ 7	73 $\pm$ 13
Vitamin C (mg)	126 $\pm$ 50	90 $\pm$ 37	45 $\pm$ 16	48 $\pm$ 11	85 $\pm$ 28	69 $\pm$ 19
Vitamin E (mg)	6 $\pm$ 4	8 $\pm$ 5	7 $\pm$ 3	7 $\pm$ 3	7 $\pm$ 2	8 $\pm$ 3
Vitamin A (RE)	638 $\pm$ 245	588 $\pm$ 246	380 $\pm$ 139	360 $\pm$ 142	509 $\pm$ 140	474 $\pm$ 140

**Notes:** Data are mean  $\pm$  SEM. No statistically significant Sex  $\times$  Condition or condition effects ( $P > 0.05$ ). Sex effect for Kcal ( $P = 0.0006$ ), protein ( $P < 0.0001$ ), carbohydrate ( $P = 0.008$ ), and fat ( $P = 0.008$ ).





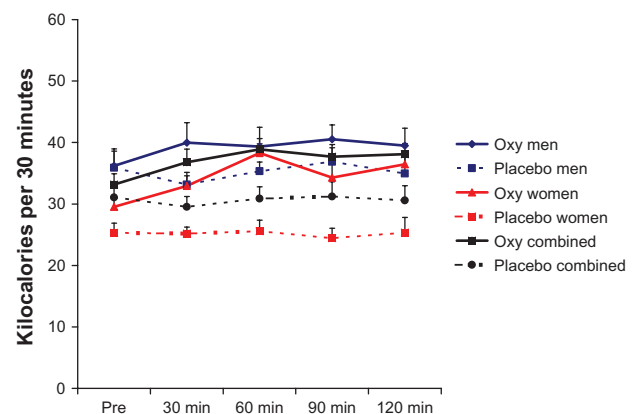
**Figure 2.** Plasma free fatty acids before and following ingestion of placebo and OxyELITE Pro™ by men and women.

**Notes:** Data are Mean  $\pm$  SEM. Sex  $\times$  Condition  $\times$  Time:  $P = 0.37$ ; Sex  $\times$  Time:  $P = 0.91$ ; Condition  $\times$  Time:  $P = 0.002$ ; Sex  $\times$  Condition:  $P = 0.004$ ; Time:  $P < 0.0001$ ; Condition:  $P < 0.0001$ ; Sex:  $P = 0.62$ ; **Area under the curve.** Sex  $\times$  Condition:  $P = 0.08$ ; Condition:  $P < 0.0001$ ; Sex:  $P = 0.85$ ; OxyELITE Pro™ Men:  $1.75 \pm 0.11 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ ; Placebo Men:  $0.65 \pm 0.16 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ ; OxyELITE Pro™ Women:  $1.51 \pm 0.07 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ ; Placebo Women:  $0.94 \pm 0.15 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ ; OxyELITE Pro™ Combined:  $1.62 \pm 0.07 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ ; Placebo Combined:  $0.78 \pm 0.12 \text{ mmol} \cdot \text{L}^{-1} \cdot 2 \text{ hr}^{-1}$ .

## Discussion

Our data indicate that the dietary supplement OxyELITE Pro™, at a dosage of two capsules, results in an increase in plasma glycerol and FFA, as well as an increase in metabolic rate. This finding is observed in both men and women who are young and healthy. Future study may include a sample of older and/or overweight individuals to determine if similar results are observed.

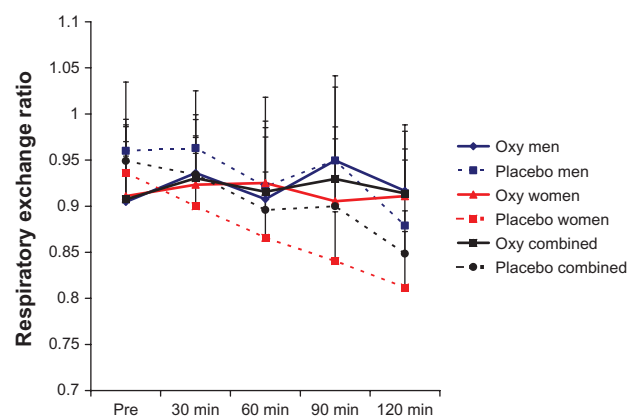
Based on the findings for increased lipolysis and metabolic rate, it might be hypothesized that the supplement may aid in weight/fat loss over time. As stated earlier, this product contains a combination of caffeine, bauhina purpurea, bacopa monniera, geranium stem extract (1,3-dimethylamylamine), cirsium oligophyllum, and rauwolfscine extract. Caffeine has lipolytic and thermogenic effects due to its ability to impair the degradation of cAMP as well as increase cAMP production via beta-adrenergic receptor independent and dependent mechanisms, respectively.<sup>9</sup> The independent effects appear due to the ability of caffeine to directly inhibit cAMP degradation, by inhibiting the cyclic nucleotide phosphodiesterase<sup>10</sup> and blocking adenosine receptors. The direct effect results from an increase in catecholamine release following caffeine ingestion, which may be secondary to the previously described adenosine inhibition.<sup>9</sup>



**Figure 3.** Kilocalorie expenditure before and following ingestion of placebo and OxyELITE Pro™ by men and women.

**Notes:** Data are mean  $\pm$  SEM. Sex  $\times$  Condition  $\times$  Time:  $P = 0.81$ ; Sex  $\times$  Time:  $P = 0.76$ ; Condition  $\times$  Time:  $P = 0.37$ ; Sex  $\times$  Condition:  $P = 0.01$ ; Time:  $P = 0.41$ ; Condition:  $P < 0.0001$ ; Sex:  $P < 0.0001$ ; **Area under the curve.** Sex  $\times$  Condition:  $P = 0.26$ ; Condition:  $P = 0.005$ ; Sex:  $P = 0.002$ ; OxyELITE Pro™ Men:  $158 \pm 10 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ ; Placebo Men:  $141 \pm 8 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ ; OxyELITE Pro™ Women:  $137 \pm 3 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ ; Placebo Women:  $101 \pm 6 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ ; OxyELITE Pro™ Combined:  $149 \pm 7 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ ; Placebo Combined:  $122 \pm 8 \text{ kcal} \cdot 2 \text{ hr}^{-1}$ .

Findings of increased metabolic rate and circulating markers of fatty acid degradation have been reported previously for caffeine alone.<sup>11–13</sup> Depending on the dosage of caffeine used, our findings generally appear similar or greater in magnitude, highlighting the potential influence of the other ingredients contained within this supplement. That being said, little is known regarding the other active ingredients, at least as pertaining to use by human subjects. For example, bauhina purpurea has been reported to have thyroid stimulating properties, with no signs of overt toxicity.<sup>14,15</sup> Thyroid hormones play an important



**Figure 4.** Respiratory exchange ratio before and following ingestion of placebo and OxyELITE Pro™ by men and women.

**Notes:** Data are mean  $\pm$  SEM. Sex  $\times$  Condition  $\times$  Time:  $P = 1.00$ ; Sex  $\times$  Time:  $P = 0.97$ ; Condition  $\times$  Time:  $P = 0.86$ ; Sex  $\times$  Condition:  $P = 0.38$ ; Time:  $P = 0.85$ ; Condition:  $P = 0.61$ ; Sex:  $P = 0.27$ .

**Table 3.** Heart rate (bpm) before and following ingestion of placebo and OxyELITE Pro™ by men and women.

Time	Men		Women		Combined	
	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo
Pre	60 ± 2	67 ± 3	72 ± 5	68 ± 4	66 ± 3	68 ± 2
30 min	55 ± 3	61 ± 3	73 ± 10	63 ± 4	64 ± 6	62 ± 2
60 min	59 ± 3	61 ± 3	79 ± 10	61 ± 4	69 ± 6	61 ± 2
90 min	61 ± 3	59 ± 2	72 ± 7	60 ± 3	67 ± 4	59 ± 2
120 min	62 ± 3	58 ± 3	79 ± 10	61 ± 4	70 ± 5	59 ± 2

**Notes:** Data are mean ± SEM. Sex × Condition × Time:  $P = 0.96$ ; Sex × Time:  $P = 0.97$ ; Condition × Time:  $P = 0.37$ ; Sex × Condition:  $P = 0.002$ ; Time:  $P = 0.77$ ; Condition:  $P = 0.02$ ; Sex:  $P = 0.0003$ .

**Table 4.** Systolic blood pressure (mmHg) before and following ingestion of placebo and OxyELITE Pro™ by men and women.

Time	Men		Women		Combined	
	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo
Pre	105 ± 3	105 ± 4	102 ± 4	97 ± 3	103 ± 2	101 ± 3
30 min	111 ± 4	106 ± 3	113 ± 9	95 ± 2	112 ± 5	101 ± 2
60 min	120 ± 5	108 ± 3	112 ± 6	97 ± 2	116 ± 4	102 ± 3
90 min	125 ± 3	109 ± 6	111 ± 5	99 ± 2	118 ± 3	104 ± 3
120 min	123 ± 4	109 ± 4	114 ± 4	96 ± 3	118 ± 3	102 ± 3

**Notes:** Data are mean ± SEM. Sex × Condition × Time:  $P = 0.70$ ; Sex × Time:  $P = 0.62$ ; Condition × Time:  $P = 0.16$ ; Sex × Condition:  $P = 0.22$ ; Time:  $P = 0.02$  (90 min and 120 min higher than pre;  $P < 0.05$ ); Condition:  $P < 0.0001$ ; Sex:  $P < 0.0001$ .

**Table 5.** Diastolic blood pressure (mmHg) before and following ingestion of placebo and OxyELITE Pro™ by men and women.

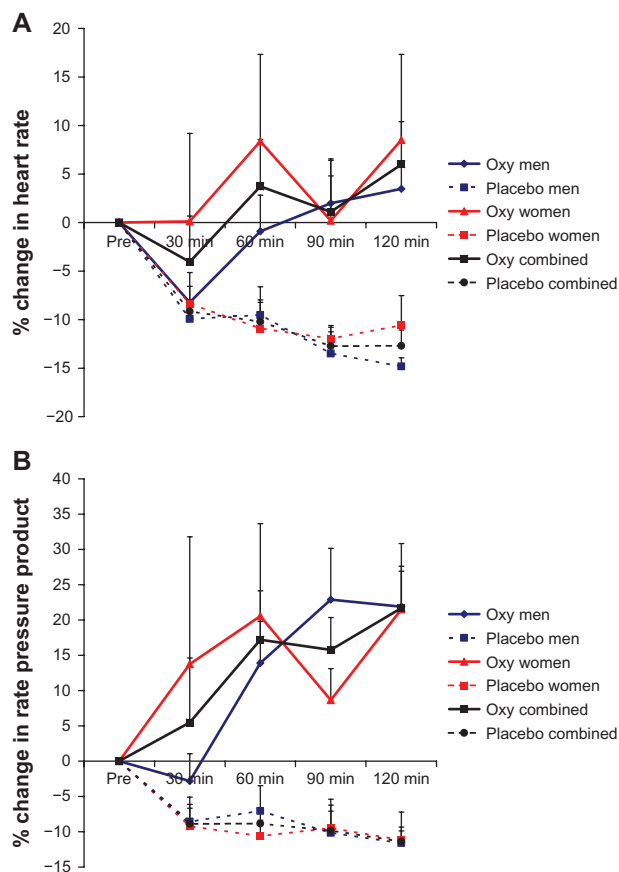
Time	Men		Women		Combined	
	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo
Pre	61 ± 4	62 ± 2	59 ± 3	60 ± 1	60 ± 2	61 ± 1
30 min	71 ± 3	67 ± 4	66 ± 4	59 ± 2	68 ± 2	63 ± 3
60 min	67 ± 4	66 ± 4	59 ± 3	56 ± 2	63 ± 3	61 ± 3
90 min	64 ± 6	65 ± 4	60 ± 4	55 ± 3	62 ± 4	60 ± 3
120 min	66 ± 3	69 ± 4	67 ± 2	58 ± 3	67 ± 2	64 ± 3

**Notes:** Data are mean ± SEM. Sex × Condition × Time:  $P = 0.72$ ; Sex × Time:  $P = 0.68$ ; Condition × Time:  $P = 0.73$ ; Sex × Condition:  $P = 0.14$ ; Time:  $P = 0.14$ ; Condition:  $P = 0.21$ ; Sex:  $P = 0.0002$ .

**Table 6.** Rate pressure product before and following ingestion of placebo and OxyELITE Pro™ by men and women.

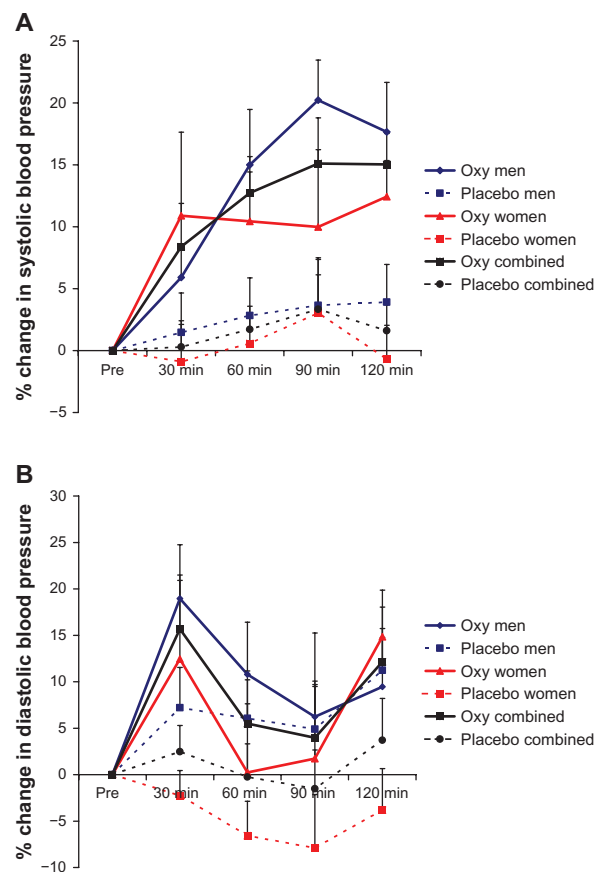
Time	Men		Women		Combined	
	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo	OxyELITE Pro™	Placebo
Pre	6258 ± 348	7163 ± 508	7304 ± 553	6594 ± 402	6781 ± 349	6878 ± 320
30 min	6083 ± 421	6514 ± 424	8615 ± 1997	5991 ± 441	7349 ± 1045	6252 ± 302
60 min	7132 ± 541	6604 ± 367	9035 ± 1579	5897 ± 403	8084 ± 846	6251 ± 281
90 min	7661 ± 516	6421 ± 551	7947 ± 700	5926 ± 288	7808 ± 417	6174 ± 306
120 min	7603 ± 453	6318 ± 437	8993 ± 1177	5848 ± 422	8298 ± 637	6083 ± 298

**Notes:** Data are mean ± SEM. Sex × Condition × Time:  $P = 0.85$ ; Sex × Time:  $P = 0.88$ ; Condition × Time:  $P = 0.24$ ; Sex × Condition:  $P = 0.004$ ; Time:  $P = 0.92$ ; Condition:  $P = 0.002$ ; Sex:  $P = 0.20$ .



**Figure 5.** Percent change from pre in heart rate (A) and rate pressure product (B) for placebo and OxyELITE Pro™.

**Notes:** Data are mean  $\pm$  SEM. **Heart rate.** Sex  $\times$  Condition  $\times$  Time:  $P = 0.78$ ; Sex  $\times$  Time:  $P = 0.88$ ; Condition  $\times$  Time:  $P = 0.02$ ; Sex  $\times$  Condition:  $P = 0.44$ ; Time:  $P = 0.31$ ; Condition:  $P < 0.0001$ ; Sex:  $P = 0.22$ ; **Rate pressure product.** Sex  $\times$  Condition  $\times$  Time:  $P = 0.40$ ; Sex  $\times$  Time:  $P = 0.66$ ; Condition  $\times$  Time:  $P = 0.006$ ; Sex  $\times$  Condition:  $P = 0.71$ ; Time:  $P = 0.58$ ; Condition:  $P < 0.0001$ ; Sex:  $P = 0.98$ .



**Figure 6.** Percent change from pre in systolic (A) and diastolic (B) blood pressure for placebo and OxyELITE Pro™.

**Notes:** Data are mean  $\pm$  SEM. **Systolic blood pressure.** Sex  $\times$  Condition  $\times$  Time:  $p = 0.50$ ; Sex  $\times$  Time:  $P = 0.58$ ; Condition  $\times$  Time:  $P = 0.07$ ; Sex  $\times$  Condition:  $P = 0.70$ ; Time:  $P = 0.003$ ; Condition:  $P < 0.0001$ ; sex:  $P = 0.10$ ; **Diastolic blood pressure.** Sex  $\times$  Condition  $\times$  Time:  $P = 0.69$ ; Sex  $\times$  Time:  $P = 0.44$ ; Condition  $\times$  Time:  $P = 0.52$ ; Sex  $\times$  Condition:  $P = 0.22$ ; Time:  $P = 0.02$ ; Condition:  $P = 0.006$ ; Sex:  $P = 0.002$ .

role in metabolic rate, with an increase in thyroid function possibly leading to an increase in energy expenditure. *Bacopa monniera* has also been reported to increase thyroid hormone,<sup>16</sup> and clinical trials have not found any adverse effects of *bacopa monniera* when consumed at a dosage of 300 mg  $\cdot$  day<sup>-1</sup>,<sup>17</sup> or as a component of a dietary supplement (BacoMind™) delivered at 300–450 mg  $\cdot$  day<sup>-1</sup>.<sup>18</sup>

The action of 1,3-dimethylamylamine appears as a simple aliphatic amine, functioning as a norepinephrine reuptake inhibitor and/or norepinephrine releasing agent, which may help explain the increase in circulating free fatty acids and glycerol with supplement ingestion. Anecdotal reports indicate a potential effect on appetite suppression and suggestions of increased weight/fat loss. However, to

our knowledge, no published reports are available pertaining to these effects in human subjects.

Pharmacological studies of *cirsium oligophyllum* reveal that the active constituent possesses  $\beta$ -adrenergic receptor agonist activity and stimulates lipolysis in subcutaneous fat cells,<sup>19</sup> possibly due to the uncoupling of protein in vitro. Uncoupling proteins are known to be involved with thermogenesis and energy dissipation. Hence, this may help explain our finding of increased energy expenditure.

Finally, rauwolscine is a stereoisomer of yohimbine and functions as an  $\alpha$ -adrenergic receptor antagonist. While rauwolscine is thought to have similar potency as yohimbine at the  $\alpha_2$ -receptor, which allows for lipolysis, it appears to be approximately 50-fold less active at the  $\alpha_1$ -receptor,<sup>20</sup> which inhibits lipolysis.





We are unaware of data pertaining to the efficacy and safety of rauwolscline use in human subjects.

Aside from the effects on metabolic rate and lipolysis, hemodynamic variables were altered in such a way as to indicate increased myocardial work. Specifically, heart rate and blood pressure were increased in response to treatment, with the obvious increase in the calculated rate pressure product. Although such changes are common with weight loss supplements,<sup>21–27</sup> in particular for those including caffeine and other stimulants, some caution should be advised when using this and similar products. This is particularly true for individuals who are hypertensive (resting blood pressure  $\geq 140/90$  mmHg) or for those who are pre-hypertensive (resting blood pressure  $\geq 120/80$  mmHg). For these individuals, it would be best to attempt weight/fat loss through both increased energy expenditure and modified/restricted dietary intake. As with the use of any weight/fat loss aid, it is prudent for individuals to be monitored by a qualified health care professional during the course of use.

## Conclusion

In conclusion, we report that the product OxyELITE Pro™ ingested at a dosage of two capsules by young and healthy men and women, resulted in an increase in plasma glycerol and FFA, in addition to metabolic rate. These results are apparent along with an increase in heart rate and blood pressure. These latter findings (increased systolic blood pressure in particular) may warrant caution, in particular in those with pre-hypertension or hypertension. The use of a lower dosage may attenuate this response. While this study only provides acute data pertaining to the lipolytic and thermogenic effects of this supplement, well-controlled intervention trials are needed in order to determine the chronic effects of the supplement on body weight/fat loss and associated metabolic and biochemical markers of health, in particular within a sample of overweight or obese subjects.

## Acknowledgments

Funding for this work was provided in part by USPlabs, LLC and the University of Memphis.

## Competing Interest

Financial support for this work was provided in part by USPlabs, LLC. None of the authors have a financial

interest in this company. RJB has received research funding or acted as consultant to other nutraceutical and dietary supplement companies. All other authors declare no competing interests.

## Authors' Contributions

CGM, TMF, REC, and RJA were responsible for data collection, blood collection and processing, data entry, and assistance with manuscript preparation. RJB was responsible for the study design, biochemical work, statistical analyses, and manuscript preparation. All authors read and approved of the final manuscript.

## Disclosures

Author(s) have provided signed confirmations to the publisher of their compliance with all applicable legal and ethical obligations in respect to declaration of conflicts of interest, funding, authorship and contributorship, and compliance with ethical requirements in respect to treatment of human and animal test subjects. If this article contains identifiable human subject(s) author(s) were required to supply signed patient consent prior to publication. Author(s) have confirmed that the published article is unique and not under consideration nor published by any other publication and that they have consent to reproduce any copyrighted material. The peer reviewers declared no conflicts of interest.

## References

1. Consitt LA, Bell JA, Houmard JA. Intramuscular lipid metabolism, insulin action, and obesity. *IUBMB Life*. 2009;61:47–55.
2. Low S, Chin MC, Deurenberg-Yap M. Review on epidemic of obesity. *Ann Acad Med Singapore*. 2009;38:57–9.
3. New Study Shows Dietary Supplement Industry Contributes More than \$60 Billion to National Economy. [http://www.naturalproductsinfo.org/index.php?src=news&srctype=detail&category=DSIB%20Releases&refno=181&view=DSIB\\_Releases\\_Detail](http://www.naturalproductsinfo.org/index.php?src=news&srctype=detail&category=DSIB%20Releases&refno=181&view=DSIB_Releases_Detail).
4. US. Weight Loss Market Worth \$46.3 Billion in 2004—Forecast to Reach \$61 Billion by 2008. <http://www.naturalnews.com/006133.html>.
5. Shim M, Saab S. Severe hepatotoxicity due to Hydroxycut: a case report. *Dig Dis Sci*. 2009;54:406–8.
6. Greenway FL. The safety and efficacy of pharmaceutical and herbal caffeine and ephedrine use as a weight loss agent. *Obes Rev*. 2001;2:199–211.
7. Saper RB, Eisenberg DM, Phillips RS. Common dietary supplements for weight loss. *Am Fam Physician*. 2004;70:1731–8.
8. Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology*. 2003;28:916–31.
9. Acheson KJ, Gremaud G, Meirim I, et al. Metabolic effects of caffeine in humans: lipid oxidation or futile cycling? *Am J Clin Nutr*. 2004;79:40–6.
10. Butcher RW, Baird CE, Sutherland EW. Effects of lipolytic and antilipolytic substances on adenosine 3',5'-monophosphate levels in isolated fat cells. *J Biol Chem*. 1968;243:1705–12.



11. Hursel R, Westerterp-Plantenga MS. Thermogenic ingredients and body weight regulation. *Int J Obes (Lond)*. 2010;34:659–69.
12. Westerterp-Plantenga MS. Green tea catechins, caffeine and body-weight regulation. *Physiol Behav*. 2010;100:42–6.
13. Westerterp-Plantenga M, Diepvens K, Joosen AM, Berube-Parent S, Tremblay A. Metabolic effects of spices, teas, and caffeine. *Physiol Behav*. 2006;89:85–91.
14. Panda S, Kar A. Withania somnifera and Bauhinia purpurea in the regulation of circulating thyroid hormone concentrations in female mice. *J Ethnopharmacol*. 1999;67:233–9.
15. Jatwa R, Kar A. Amelioration of metformin-induced hypothyroidism by Withania somnifera and Bauhinia purpurea extracts in type 2 diabetic mice. *Phytother Res*. 2009;23:1140–5.
16. Kar A, Panda S, Bharti S. Relative efficacy of three medicinal plant extracts in the alteration of thyroid hormone concentrations in male mice. *J Ethnopharmacol*. 2002;81:281–5.
17. Nathan PJ, Clarke J, Lloyd J, Hutchison CW, Downey L, Stough C. The acute effects of an extract of Bacopa monniera (Brahmi) on cognitive function in healthy normal subjects. *Hum Psychopharmacol*. 2001;16:345–51.
18. Pravina K, Ravindra KR, Goudar KS, et al. Safety evaluation of BacoMind in healthy volunteers: a phase I study. *Phytomedicine*. 2007;14:301–8.
19. Mori S, Satou M, Kanazawa S, et al. Body fat mass reduction and up-regulation of uncoupling protein by novel lipolysis-promoting plant extract. *Int J Biol Sci*. 2009;5:311–8.
20. Perry BD, U'Prichard DC. [3H]rauwolscine (alpha-yohimbine): a specific antagonist radioligand for brain alpha 2-adrenergic receptors. *Eur J Pharmacol*. 1981;76:461–4.
21. Bui LT, Nguyen DT, Ambrose PJ. Blood pressure and heart rate effects following a single dose of bitter orange. *Ann Pharmacother*. 2006;40:53–7.
22. Haller CA, Jacob P 3rd, Benowitz NL. Enhanced stimulant and metabolic effects of combined ephedrine and caffeine. *Clin Pharmacol Ther*. 2004;75:259–73.
23. Haller CA, Benowitz NL, Jacob P 3rd. Hemodynamic effects of ephedra-free weight-loss supplements in humans. *Am J Med*. 2005;118:998–1003.
24. Vukovich MD, Schoorman R, Heilman C, Jacob P 3rd, Benowitz NL. Caffeine-herbal ephedra combination increases resting energy expenditure, heart rate and blood pressure. *Clin Exp Pharmacol Physiol*. 2005;32:47–53.
25. Bloomer RJ, Canale RE, Blankenship MM, Hammond KG, Fisher-Wellman KH, Schilling BK. Effect of the dietary supplement Meltdown on catecholamine secretion, markers of lipolysis, and metabolic rate in men and women: a randomized, placebo controlled, cross-over study. *Lipids Health Dis*. 2009;8:32.
26. Bloomer RJ, Fisher-Wellman KH, Hammond KG, Schilling BK, Weber AA, Cole BJ. Dietary supplement increases plasma norepinephrine, lipolysis, and metabolic rate in resistance trained men. *J Int Soc Sports Nutr*. 2009;6:4.
27. Hoffman JR, Kang J, Ratamess NA, Rashti SL, Tranchina CP, Faigenbaum AD. Thermogenic effect of an acute ingestion of a weight loss supplement. *J Int Soc Sports Nutr*. 2009;6:1.

**Publish with Libertas Academica and every scientist working in your field can read your article**

*"I would like to say that this is the most author-friendly editing process I have experienced in over 150 publications. Thank you most sincerely."*

*"The communication between your staff and me has been terrific. Whenever progress is made with the manuscript, I receive notice. Quite honestly, I've never had such complete communication with a journal."*

*"LA is different, and hopefully represents a kind of scientific publication machinery that removes the hurdles from free flow of scientific thought."*

**Your paper will be:**

- Available to your entire community free of charge
- Fairly and quickly peer reviewed
- Yours! You retain copyright

**<http://www.la-press.com>**